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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 08/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/666,072	COURTIN ET AL.	
	Examiner	Art Unit	
	David Lukton	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/11/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the directives of the response filed 6/14/05, claims 28-31 and 33 have been cancelled. Claims 34-43 remain pending.

Applicants arguments filed 6/14/05 have been considered and found not persuasive.

Claims 34-42 are now rejoined with the elected group.

✧

The abstract is objected to. The compounds referred to in the abstract are not the same as those claimed.

✧

The specification is objected to. On page 21, the following is recited (in two locations):

"Spectrum RMN $CDCl_3$ "

This should instead be the following:

NMR Spectrum *($CDCl_3$)*

✧

Claim 43 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 or 2 of U.S. Patent No. 6,677,429. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 43 is a narrow subgenus of claim 1 of the patent.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application . See 37 CFR 1.78(d).

✦

35 U.S.C. §101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture or composition of matter or any new and useful improvement therof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claim 37 is rejected under 35 USC §101 because the claimed invention is not supported by a well established utility.

Claim 37 recites that mycosic ailments can be "prevented". However, there is no evidence that the case. Even if applicants have provided extensive human clinical data on thousands of AIDS patients, this would not establish that prevention can be achieved. If the compound were administered to each of 10,000 AIDS patients, and of these, just one developed a mild case of "athletes foot" (caused by a fungus), such a result would be wildly successful by any standard. Yet this result would actually establish that prevention had not been achieved. It is suggested that the term "prevention" be avoided in the claims.

Claim 37 is also rejected under 35 USC §112 first paragraph. Specifically, since the claimed invention is not supported by a well established utility for the reasons

set forth above, one skilled in the art clearly would not know how to use the claimed invention.

✧

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 43 recites that R_2 is an alkyl of 2 carbons "interrupted with" $-NH_2$. There is probably descriptive support for the alkyl being substituted with $-NH_2$, but there does not appear to be support for R_2 being an alkyl of 2 carbons "interrupted with" $-NH_2$.

✧

Claims 34-43 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants have proposed an assay on page 22 of the specification, but no data is presented. Accordingly, it may well be the case that the claimed compounds are inactive. As it happens, one cannot "predict" antifungal efficacy merely by viewing the structure of a compound.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

Accordingly, "undue experimentation" would be required to practice the claimed invention.

Applicants have not responded to this ground of rejection, and so it is maintained without further comment. If applicants would like to advance the prosecution, it suggested that they explain why it is that the skilled mycologist would believe that the claimed compounds can indeed inhibit fungal growth.

In the event that applicants can show inhibition of fungal growth *in vitro*, the next question will be whether or not fungal infections in a human (or animal) subject can be successfully treated. Consider the following references:

- Buchta, V. (*Mycoses* **44** (11-12) 505-12, 2001) discloses that a patient died from a fungal infection despite being treated with compounds that

exhibit anti-fungal activity *in vitro*.

- Adam (*Medicine* **65**, 203, 1986) discloses (page 208, col 2) that *in vitro* susceptibility to antifungal agents did not correlate with therapeutic efficacy of the agents.

- Nagasawa M. (*Journal of Infection* **44** (3) 198-201, 2002) discloses that a patient died from a fungal infection despite being treated with compounds that exhibit anti-fungal activity *in vitro*.

- Manfredi R (*Mycopathologia* **148** (2) 73-8, 1999) discloses that two patients died from a cyrotpococcus infection despite being treated with an agent that exhibited anti-fungal activity *in vitro*.

- Wang M. X. (*Cornea* **19** (4) 558-60, 2000) discloses that a patient was treated with an agent that exhibited anti-fungal activity *in vitro*, but that despite this, his fungal sclerokeratitis progressed to endophthalmitis.

- Bhalodia M V (*Journal of the Association for Academic Minority Physicians* **9** (4) 69-71, 1998) discloses that a compound that exhibited anti-fungal activity *in vitro* was not effective to treat a candida infection in a patient.

- Moore M. L. (*Journal of Perinatology* **21** (6) 399-401, 2001) discloses that a premature infant died from a fungal infection despite being treated with a compound that exhibits anti-fungal activity *in vitro*.

- Berman, Judith (*Nat Rev Genet* **3** (12) 918-30, 2002) discloses that many immunocompromised patients die from *Candida* infections in spite of having received various dosages of compounds which exhibit anti-fungal activity *in vitro*.

- van Duin, David (*Antimicrobial Agents and Chemotherapy* **46** (11) 3394-400, 2002) has disclosed an example of a compound which exhibits antifungal activity *in vitro* but not *in vivo*.

- Marr K. A. (*Antimicrobial Agents and Chemotherapy* 45 (1) 52-9, 2001) discloses that a patient developed a fungal infection despite prophylactic

treatment with a compound which exhibits antifungal activity *in vitro*.

In accordance with the foregoing, one cannot "predict" therapeutic efficacy on the basis of fungal growth inhibition *in vitro*. In addition, claim 34 is not limited to treatment of fungal infections. Rather, claim 34 asserts that any ailment can be successfully treated, provided that that ailment was caused, directly or indirectly by exposure to a fungus. One point to be made is that bacteria and fungi often occur together; thus if a person is exposed to a mixture of fungi and bacteria, he is likely to develop both a fungal infection and a bacterial infection. However, even if applicants can show that fungal infections can be successfully treated, it will not follow therefrom that bacterial infections can be successfully treated. Similarly, parasites often coexist with fungi.

Clearly, "undue experimentation" would be required to practice the claimed invention.

✧

Claims 34-43 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 34 recites a method of treating an ailment in "people". This implies that treatment of a single human subject is excluded. Is this intended? See also claim 37.

- Claim 34 is indefinite as to the ailments that might be intended.

- In claim 36, the terms "aspergilloses" and "cryptococcoses" are used. Here, the singular is preferable (i.e., *aspergillosis* and *cryptococcosis*).

- Claim 36 makes reference to "invasive aspergilloses of immunocompromise". However, there is no such disease *per se*. Certainly, immunocompromised patients are subject to infection by fungi. But the phrase at issue is not a specific disease in and of itself. Either of the following would be better than what is currently recited: *invasive aspergillosis in an immunocompromised patient* or *invasive aspergillosis in an immunocompromised subject.*
  Better still would be to create a new claim and recite the following:

  50. *The method of claim 34 wherein the subject is immunocompromised, and wherein the ailment is invasive aspergillosis.*

- Claim 35 recites the following: "krusei, tropicalis, pseudotropicalis, parapsilosis". However, these names are incomplete. Perhaps what is intended is the following: *Candida krusei, Candida tropicalis, Candida pseudotropicalis, Candida parapsilosis*

- Claim 38 recites the following: "said derivative of echinocandin B" . This phrase lacks antecedent basis.

- Claim 38 recites that the compound in question is administered not as such, but rather as a composition. Accordingly, claim 38 is not properly dependent on claim 34 or on claim 43, since both of these claims (34 and 43) are drawn to a compound or to a method of using a compound. One option would be to create a new claim which is drawn to a composition. Claims 38-39 could then be made dependent on this composition claim. The same issue applies in the case of claims 41 and 42.

- Claim 39 recites the following: "said derivative of echinocandin B" . This phrase lacks antecedent basis.

- Claim 41 recites the following: "said derivative of a compound of claim 43". This phrase lacks antecedent basis.

- In claim 43, the structural formula bears a group designated "R", which is defined as a specific isomer of octyloxybiphenylcarbonyl. However, a substituent variable must encompass multiple possibilities, otherwise it is

not a variable. It is suggested that "R" be eliminated from formula III (claim 43), and that the definition of "R" be eliminated as well.

- In claim 43, R_3 can correspond to just one substituent group. Accordingly, R_3 should be eliminated from the claim. The same applies to variables "Z" and R_4.

- In claim 43, the following is recited: "R2 is an alkyl of two carbons interrupted with". At a distance of about 1 inch above this phrase, one finds the functional group "$-NH_2$". The issue is that it may be unclear to the persons responsible for printing the final document that the "$-NH_2$" is supposed to be the group that the alkyl (of R2) is to be interrupted with. The following can be used:

  R_2 is an alkyl of two carbons substituted with $-NH_2$.

- In claim 43, variables "T", "Y" and "W" are defined, but do not appear in the structural formula.

- In claim 43, variables R_2, R_3 and R_4 are recited, wherein the number (2, 3 or 4) appears as a subscript. In the definition of the variables, none of variables R_2, R_3 and R_4 is defined. Instead, variables R2, R3 and R3 have been defined. Consistency should be maintained.

- In claim 43, the phrase "or a pharmaceutically acceptable acid addition salt" should be preceded by a semicolon.

✦

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at (571)272-0974. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.